

## Remarks

### Claim status

Claims 1-6, 9-12, and 18-21 were pending in this Application. Claims 1-6, 9-12, and 18-21 stand rejected on arguments laid out in the Office Action mailed June 11, 2009.

### Amendments to the specification

In the present Amendment, the Sequence Listing has been amended to list sequences shown in Figures 10, 13, and 14 that had been inadvertently omitted in the previously filed Sequence Listing.

Therefore, Applicant submits that no new matter is added by these amendments.

### Amendments to the claims

Claims 1-4, 9, 12 and 18 are amended by the present amendment without any intent of disclaiming canceled subject matter or equivalents thereof. Claims 1 and 12 are amended to correct an inadvertent error in the spelling of “glioblastoma multiforme.” Claims 1 and 9 are amended without prejudice to remove recitation of SEQ ID NOs 8 and 13 and to make claim language consistent. The claims have also been amended to focus prosecution on embodiments in which temozolomide is the second agent.

Claims 5, 6, 10, 11, 19, 20, and 21 are canceled by the present amendment without prejudice.

New claims 22-28 are added. New claims 22-28 refer to embodiments in which the chlorotoxin comprises an incorporated radioactive isotope, which is supported by the specification as originally filed. (See, *e.g.*, page 22, lines 16-28.) New claim 25 recites methods comprising administering chlorotoxin as a first agent. Support for new claim 25 can be found in the specification as originally filed, *inter alia*, beginning on page 8 (at line 29) through page 9 (at line 14); on page 22 (lines 17 through 28); and on page 24 (line 33). Applicants submit that the present Amendment introduces no new matter.

After entrance of the present Amendment, claims 1-4, 9, 12, 18, and 22-28 are pending and are presented for examination.

### Priority claim

The Examiner has asserted that claims 1, 9, and dependents therefrom (before the instant amendments) did not find full support in priority applications 60/384,171 and 60/406,033 because the claims recited SEQ ID NO: 13, the sequence of which was not recited *ipsissimis verbis*. The Examiner has therefore determined that a priority date of June 2, 2003 is to be used for the instant claims.

Without acquiescing to the Examiner's assertions regarding the priority claim, Applicants have amended claims 1 and 9 and dependents therefrom such that they only refer to SEQ ID NOs: 1-7, each of which finds unambiguous *ipsissimis verbis* support in both priority applications (60/384,171 and 60/406,033). Applicants respectfully submit that claims 1-4, 9, 12, 18 and 19 (as amended) and new claims 22-28 find full support in the priority applications. Accordingly, a priority date of May 31, 2002 should be used for claims 1-4, 9, 12, 18, 19, and 22-28.

### Claim objections

The Examiner has objected to claims 1, 6, 11, and 12 because of informalities relating to inadvertent typographical errors in the spelling of the term 'glioblastoma multiforme' and to use of the abbreviation 'BCNU' in the claims. Applicants have amended claims 1 and 12 to correct the error and have cancelled claims 6 and 11, the only claims to have recited BCNU.

### Specification objections

The Examiner has objected to the disclosure because of informalities relating to sequences shown in Figures 10, 13, and 14 without sequence identifiers. Amended drawings are submitted herewith to correct these informalities.

### Previous rejections

The previous rejections under 35 U.S.C. § 112, first paragraph and 35 U.S.C. § 102 appear to have been overcome by Applicants' amendment and response filed on February 27, 2009.

### Claim rejections – 35 USC 103

Claims 1-6, 9-12, and 18-21 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Samoylova *et al.*<sup>1</sup> and Stupp *et al.*<sup>2</sup> *et al.*. Samoylova *et al.* teaches phage-derived peptides for recognition and targeting of glial cell tumors. Stupp *et al.* teaches administration of temozolomide for brain tumours and glioma.

As explained in the response to Office Action filed on February 27, 2009, Samoylova *et al.* *explicitly and strongly teaches away* from the claimed invention. Despite such an explicit and strong teaching away from the claimed invention, the Examiner continues to argue that “one would have been motivated to combine the chemotherapeutic agent temozolomide as taught by Stupp into the method/compositions of Samoylova since both references deal with therapeutics specifically of brain tumors. Both references motivate the use of combination therapies.”

Applicants respectfully traverse to the extent, if any, that the rejections are maintained over the claims as amended. As an initial matter, the Examiner seems to suggest that a general motivation to use a combination therapy suffices to render the claimed invention obvious. However, a general motivation to use combination therapy, *even if* provided by either or both of the references, fails to render obvious using chlorotoxin or a chlorotoxin derivative as a first agent specifically in combination with temozolomide as a second agent, as recited by the present claims. Furthermore, that both references “deal with therapeutics specifically of brain tumors” does not suffice as a motivation to combine the therapies taught in each reference.

In responding to Applicants’ arguments regarding Samoylova *et al.*, the Examiner has mischaracterized or misunderstood the teachings of Samoylova *et al.*. For example, on page 11 of the Office Action, the Examiner has asserted that “one would be motivated to use chlorotoxin as the peptide of the instant invention” (the invention described in Samoylova *et al.*) and has applied the teachings of Samoylova *et al.* regarding *the synthetic peptides taught by Samoylova et al.* as though they applied to chlorotoxin. The Examiner’s misapplication of the teachings of Samoylova *et al.* forms the basis of the Examiner’s obviousness rejection.

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<sup>1</sup> US 2003/0216322

<sup>2</sup> The Lancet v2 Sept 2001 552-560

As mentioned previously, Samoylova *et al.* mentions chlorotoxin in the context of other known molecules that have been used to target gliomas (see paragraph [0010]) and then *disparages chlorotoxin* and other known molecules as targeting agents. The central premise of the utility of the invention described in Samoylova *et al.* is that *novel peptides* that bind to gliomas are needed. Thus, the Examiner's assertion that "one would be motivated to use chlorotoxin as the peptide of the instant invention" is illogical.

For all these reasons, there is no teaching or suggestion in Samoylova *et al.* to combine chlorotoxin with any other chemotherapeutic.

Stupp *et al.* does not cure the deficiency in Samoylova *et al.* As explained previously, no motivation is provided by Stupp *et al.* to combine chlorotoxin with any another therapeutic, and certainly no motivation is provided to combine chlorotoxin with temozolomide. Stupp *et al.* does not even mention chlorotoxin or chlorotoxin derivatives, despite extensively discussing other therapies that may be combined with temozolomide (*e.g.*, radiotherapy, nitrosureas, procarbazine, and irinotecan). Applicants respectfully note that none of the therapies mentioned by Stupp *et al.* are even similar to chlorotoxin or a chlorotoxin derivative, which is a peptide.

No combination of these two references could render obvious the claimed invention. Applicant respectfully requests removal of this rejection.

#### Double patenting

Claims 1-6 and 18-21 stand *provisionally* rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 42-49 of copending Application No. 10/522,810 in view of Stupp *et al.* and Samoylova *et al.*.

Claims 1-6, 9-12, and 18-21 stand *provisionally* rejected in the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 4, 11, and 30-48 of copending Application No. 11/731,661 in view of Samoylova *et al.* and Stupp *et al.*.

Claims 1-6, 9-12, 18-21 stand *provisionally* rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 4 and 21 of copending Application No. 11/547,875 in view of Stupp *et al.* and Samoylova *et al.*

To the extent, if any, that these provisional rejections apply to the claims as amended, Applicants respectfully request that these provisional rejections be held in abeyance until the

presently pending claims are deemed otherwise allowable. Applicants have not yet addressed these rejections as they are provisional rejections and will consider, if appropriate, filing appropriate terminal disclaimers when the presently pending claims are deemed otherwise allowable. Applicants respectfully note, however, that a proper double patenting rejection is based on a claim-by-claim comparison and that none of the claims in other patent applications cited as a basis for the provisional double patenting rejections refer specifically to temozolomide.

### Conclusion

For all of these reasons, the rejections are not applicable to the claims and the claims should be allowed. A Notice to that effect is earnestly solicited.

Applicants believe that they have paid all fees due with this response. Should any additional fees be required to maintain pendency and/or to protect the filing date of this application, please consider this a conditional petition therefore and authorization to debit Deposit Account No. 03-1721, referencing Attorney Docket No. 2006636-0026. No authorization is provided to charge *optional* fees (*e.g.*, claims fees); should the PTO be of the view that additional fees are required, a Notice to that effect is respectfully requested.

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